DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 11/25/2011 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 05/25/2011 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 11/25/2011, claims 1, 3, 4, 33, 39 and 87-90 are under examination and claims 19, 21-22, 27, 34-36, 40-63 and 91-108 are withdrawn from further consideration as being drawn to a non-elected invention.

New Claim Rejections – necessitated by amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 33, 39 and 87-90 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1, 3, 4, 33, 39 and 87-90 recite the new limitation wherein "the adenosines and guanosines of the sense strand are 2'-ribonucleotides".

Applicant states in the Remarks filed 11/25/2011 that support for this limitation can be found in the specification as originally filed. A search of the instant specification does not reveal this specific limitation in the context of the claimed siRNA comprising the modifications as listed in claim 1 and having the claimed function of enhanced in vivo stability.

If Applicant believes that such support is present in the specification and claimed priority documents, Applicant should point, with particularity, to where such support is to be found.

Claim Rejections - 35 USC § 103

Claims 1, 3, 4, 33, 39 and 87-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over McSwiggen et al. (US 2004/0192626 of record) is maintained for the reasons of record.

The claims have been amended to include a new limitation wherein "the adenosines and guanosines of the sense strand are 2'-ribonucleotides".

Applicant's arguments filed 11/25/2011 have been fully considered but they are not persuasive. Applicant argues McSwiggen et al. fails to teach or suggest the now

claimed siRNA wherein the adenosines and guanosines of the sense strand are 2'-ribonucleotides.

McSwiggen et al. exemplifies a siRNA wherein the pyrimidines are substituted with 2'- fluoro groups on the sense and antisense strands and the adenosines and guanosines of the sense strand are 2'-ribonucleotides and teach the antisense strand has an adenosine and/or guanosine within 2 nucleotides upstream or 9 nucleotides downstream of the cleavage site (see Figure 19C).

McSwiggen et al. do not exemplify an siRNA wherein the antisense strand is modified with a 2'-deoxy adenosine or guanosine within 2 nucleotides upstream or 9 nucleotides downstream of the cleavage site, however given McSwiggen et al. teach the antisense (and/or the sense) strand can comprise combinations of modified nucleotides such as 2'-deoxy groups, it would have been obvious and within the realm of ability of one of ordinary skill in the art to make said modifications.

At paragraph [0011-0012], McSwiggen et al. teach the introduction of chemically modified nucleotides provide a powerful means to overcome the limitations of in vivo stability and bioavailability inherent to native RNA molecules and teach the modified siRNA molecules have increased stability but are able to still mediate RNAi (see paragraph 0111). McSwiggen et al. teach the siRNA molecule has a cleavage site for RISC which mediates cleavage of the target gene (see paragraph 0005) and references the work of Elbashir et al. (Genes and Dev 2001 also cited on IDS filed 02/27/2006) which identifies the cleavage region of siRNA.

McSwiggen et al. do not specifically teach the siRNA comprising modified nucleotides retains the ability to inhibit expression of the target mRNA by at least 30% however beginning at paragraph [0315] McSwiggen et al. teach optimizing the activity of the siRNA comprising modified nucleotides to preserve the ability of the siRNA to mediate RNAi efficiently in cells. It would have been obvious to one of ordinary skill in the art to synthesize a siRNA comprising chemically modified nucleotides as taught above and optimize the incorporation of said modifications to obtain a siRNA with the highest ability to inhibit the desired gene expression.

Beginning in Example 1, McSwiggen et al. teach detailed steps on constructing the said siRNA molecules and methods of testing the activity of said siRNA against the target gene. Given that McSwiggen et al. teach the introduction of chemically modified nucleotides provides a powerful means to overcome the limitations of in vivo stability and bioavailability inherent to native RNA molecules, one would have clearly incorporated said modifications into a siRNA and would have optimized the position and number of modified nucleotides to obtain a siRNA with the highest ability to inhibit the desired gene expression. Moreover, given that there are a multitude of general methods and strategies to determine the location of incorporation of chemically modified nucleotides as taught by McSwiggen et al., one of ordinary skill in the art would have expected to be able to determine the location of incorporation of chemically modified nucleotides as instantly claimed while maintaining the siRNAs ability to inhibit gene expression by at least 30%.

Thus, the invention as a whole would have been prima facie obvious to one of skill in the art at the time the invention was made.

Response to Arguments

Claim Rejections - 35 USC § 103

The rejection of claims 1, 3, 4, 33, 39 and 87-90 under 35 U.S.C. 103(a) as being unpatentable over McSwiggen et al. (US 2004/0192626 of record) is withdrawn in view of the new grounds of rejection above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KIMBERLY CHONG whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact the SPE for 1635 Heather Calamita at 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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